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HIGH PRODUCTION VOLUME (HPV) CHALLENGE PROGRAM

TEST PLAN

FOR

6-Amino-4-chloro-m-toluenesulfonic acid (2B Acid)

(CAS NO.: 88-51-7)

and

2-Amino-5-chloro-p-toluenesulfonic acid (C Amine)

(CAS NO.: 88-53-9)

PREPARED BY:

COLOR PIGMENT MANUFACTURERS ASSOCIATION, INC.

MONOAZO AND RELATED PIGMENTS COMMITTEE

MONOAZO INTERMEDIATES TASK FORCE

June, 2006

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OVERVIEW

The Monoazo and Related Pigments Committee ("MRPC") and the Monoazo Intermediates Task Force of the Color Pigment Manufacturers Association, Inc. (CPMA) and its member companies hereby submits for review and public comment the test plan for 6-Amino-4-chloro-m-toluenesulfonic acid (2B Acid) (CAS NO.: 88-51-7) and 2-Amino-5-chloro-p-toluenesulfonic acid C Amine) under the Environmental Protection Agency's (EPA) High Production Volume (HPV) Challenge Program. It is the intent of the MRPC and its member companies to use existing data and predictive computer models to adequately fulfill the Screening Information Data Set (SIDS) for the various physicochemical, environmental fate, ecotoxicity test, and human health effects endpoints.

6-Amino-4-chloro-m-toluenesulfonic acid (2B Acid) (CAS NO.: 88-51-7) and 2-Amino-5-chloro-p-toluenesulfonic acid C Amine) (CAS NO. 88-53-9) are stable solids. These chemicals are used as closed system intermediates in the production of color pigments.

TEST PLAN SUMMARY

CAS No.s 88-51-7 and 88-53-9	Information	OECD Study	Other	Estimation	GLP	Acceptable	New Testing Req.
STUDY	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
PHYSICAL-CHEMICAL DATA							
Melting Point	Y	Y	-	Y	N	Y	N
Boiling Point	N/A	-	-	Y	N	Y	N
Vapor Pressure	Y	-	-	Y	N	Y	N
Partition Coefficient	Y	-	-	Y	N	Y	N
Water Solubility	Y	Y	-	Y	Y	Y	N
ENVIRONMENTAL FATE ENDPOINTS							
Photodegradation	Y	N	-	Y	N	Y	N
Stability in Water	N/A	Y			Y	Y	N
Biodegradation	Y	Y	Y	-	Y	Y	N
Transport between Environmental Compartments (Fugacity)	Y	Y	-	Y	N	Y	N
ECOTOXICITY							
Acute Toxicity to Fish	Y	Y	-	-	Y	Y	N
Acute Toxicity to Aquatic Invertebrates	Y	Y		-	Y	Y	N
Toxicity to Aquatic Plants	Y	Y		-		Y	N
TOXICOLOGICAL DATA							
Acute Toxicity	Y	Y	Y	-	Y	Y	N
Repeated Dose Toxicity	Y	Y		-	Y	Y	N
Genetic Toxicity – Mutation	Y	Y	Y	-	Y	Y	N
Genetic Toxicity – Chromosomal Aberrations	Y	Y	Y	-	Y	Y	N
Developmental Toxicity	Y	Y		-	Y	Y	N
Toxicity to Reproduction	Y	Y		-	Y	Y	N

TEST PLAN DESCRIPTION FOR EACH SIDS ENDPOINT

A. Physicochemical

Melting point -	A value for this endpoint was obtained from measurements and through surrogate data for 4B Acid.
Boiling Point -	A value for this endpoint was obtained using a computer estimation-modeling program within EPIWIN and through surrogate data for 4B Acid.
Vapor Pressure -	A value for this endpoint was obtained using a computer estimation-modeling program within EPIWIN and through surrogate data for 4B Acid.
Partition Coefficient -	A value for this endpoint was obtained using a computer estimation-modeling program within EPIWIN and through surrogate data for 4B Acid.
Water Solubility -	A value for this endpoint was obtained using a computer estimation-modeling program within EPIWIN. A value for this endpoint was also obtained from analysis of a surrogate substance 4B Acid.

Conclusion: All end points have been satisfied by utilizing data obtained from the various physical chemical data modeling programs within EPIWIN or using measured values. The results of the various computer estimation models within EPIWIN have been noted by the Agency as acceptable in lieu of actual data or values identified from textbooks. No new testing is required.

B. Environmental Fate

Photodegradation -	A value for this endpoint was obtained using AOPWIN, a computer estimation-modeling program within EPIWIN (1)
Stability in Water -	A value for this endpoint was obtained from analysis of a surrogate substance 4B Acid
Biodegradation -	This endpoint was satisfied through the use of an OECD-301C test for 4B Acid.
Fugacity -	A value for this endpoint was obtained using the EQC Level III partitioning computer estimation model within EPIWIN.

Conclusion: All endpoints have been filled with data utilizing acceptable methodologies and of sufficient quality to fulfill these endpoints. No new studies are being proposed.

C. Ecotoxicity Data

Acute Toxicity to Fish -	This endpoint is filled by data from a study that followed the OECD TG-203 protocol and was conducted under GLP assurances for the surrogate substance 4B Acid.
Acute Toxicity to Aquatic Invertebrates -	This endpoint is filled by data from a study that followed the OECD TG-202 protocol and was conducted under GLP assurances for the surrogate substance 4B Acid.
Toxicity to Aquatic	This endpoint is filled by data from a study that followed the OECD TG-201 protocol
Bioaccumulation	This endpoint is filled by data from a GLP study for the surrogate substance 4B Acid.

Conclusion: All endpoints have been satisfied with surrogate data from studies that were conducted using established OECD guidelines. In total, these currently available studies are of sufficient quality to conclude that no additional testing is needed.

D. Toxicological Data

Acute Toxicity -

This endpoint is filled by oral exposure data from various published and unpublished references to studies. Data are also available from a OECD TG 407 study for the surrogate substance 4B Acid.

Repeat Dose Toxicity -

This endpoint is filled by data from a study that followed OECD TG-407 for the surrogate substance 4B Acid.

Genetic Toxicity

This endpoint is filled by published and unpublished values supplied by manufacturers and data from a study that followed OECD TG-471 and 472 for the surrogate substance 4b Acid.

ation -

ration -

This end point is filled by published values supplied by manufacturers and data from a study that followed OECD TG-473 for the surrogate substance 4B Acid.

**Developmental
Toxicity -**

This endpoint is filled by data from a study that followed OECD TG-421 for the surrogate substance 4B Acid

**Reproductive
Toxicity -**

This endpoint is filled by data from a study that followed OECD TG-421 for the surrogate substance 4B Acid.

Conclusion:

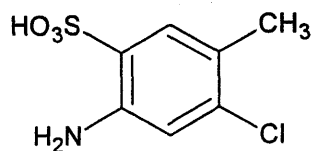
All endpoints have been satisfied with data which are of sufficient quality to conclude that no additional testing is needed.

Rationalization for Use of Surrogate Data

As a means of reducing the number of tests that may be conducted, the EPA allows for the use of data from structurally similar compounds to characterize specific SIDS endpoints (US EPA 1999a). Accordingly, the MRPC believes that data from the available studies for 4B Acid meets the needed criteria for use as a surrogate in the completion of some SIDS endpoints. All three of these color pigment intermediates, 2B Acid, 4B Acid and C Amine share similar structures, characteristics and functions. As is readily seen by their structures below, 2 B Acid, 4 B acid, and C Amine only differ by the presence of a single chlorine atom in the fourth or fifth position, the position of the amino group and position of the toluenesulfonic acid group. These modifications do not significantly alter the basic physicochemical properties or the basic biological effects. All three compounds have a similar acute toxicity value. Accordingly, data from 4B Acid has been used to fulfill a number of the SIDS endpoints. All three compounds are used as closed system intermediates in the production of azo color pigments.

Common Name: 2B Acid

Structure:



CAS 88-51-7

Chemical Name: 6-Amino-4-chloro-m-toluenesulfonic acid

Melting Point: 330 °C

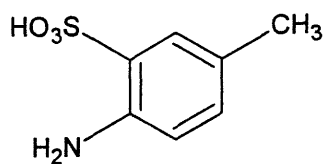
Boiling Point: Solid powder

Density

Acute Toxicity: LD50>12,300 mg/kg (RTECS)

Common Name 4B Acid

Structure:



CAS 88-44-8

Chemical Name 4-Amino-m-toluenesulfonic acid

Melting Point >300 °C

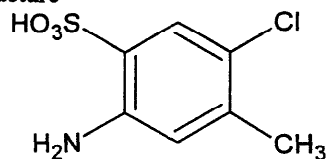
Boiling Point: Solid powder

Density 1.49 g/cubic centimeter

Acute Toxicity: LD50>2000 mg/kg

Common Name C Amine

Structure



CAS 88-53-9

Chemical Name 2-Amino-5-chloro-p-toluenesulfonic acid

Melting Point 283.5 °C estimate MPBPWIN v. 1.40

Specific Gravity (water = 1): 0.70

Acute Toxicity: LD50>5000 mg/kg, NPIRI, OECD TG 401 LD50 > 5,000 mg/kg

Water Solubility : OECD TG 105 8.9 mg/l at 25 °C

SIDS DATA SUMMARY

Physical Chemical Endpoints

Data assessing the various physicochemical properties (melting point, boiling point, vapor pressure, partition coefficient, and water solubility) for C Amine and 2B Acid were also obtained from estimations using the models within EPIWIN. These data indicate that both substances are stable solids at room temperature, are largely soluble in water.

Environment

For the environment, analysis of 4B Acid indicates that: This substance is soluble in water (6.0 g/L at 20°C) and the vapor pressure is low (< 0.00052 Pa at 100°C) [OECD TG104]. This substance was not readily biodegradable (0% after 14 days on BOD) [OECD TG301C] and is stable to hydrolysis in water at pH 4, 7 and 9 [OECD TG111]. The bioconcentration potential is low (BCF < 4 (0.2 mg/L) and < 0.4 (2 mg/L)) [OECD TG305C]. The log Pow is -0.67 at 25°C [OECD TG107]. This substance, if released into the atmosphere, will react with photochemically produced hydroxyl radical and decrease with a half-life of 4.5 hours. The pKa value of this substance is 3.28. It is present as a zwitterion under environmental condition. The behavior of this substance in the environment is considered to be similar to a weak acid.

The fugacity model (Mackay level III) suggests that if released to water, the majority of the substance would remain in the water compartment and, if released into air or soil, ca.50% would distribute to both water and the soil compartment. In an acute toxicity test to fish, the LC50 was greater than 10 mg/L (*Oryzias latipes*, 96hr limit test) [OECD TG203]. In an acute toxicity test to daphnia, the EC50 was greater than 10 mg/L (*Daphnia magna*, 48hr limit test) [OECD TG202]. In an acute toxicity test to algae, the EC50 was greater than 10 mg/L (*Selenastrum capricornutum*: 0 – 72 hr biomass, and 24 – 72 hr growth rate) [OECD TG201]. In a chronic toxicity test to daphnia, the NOEC was 3.2 mg/L (*Daphnia magna*, 21 days reproduction) [OECD TG211] and in a chronic toxicity test to algae, the NOEC was 10 mg/L (*Selenastrum capricornutum*: 0 – 72 hr biomass, and 24 – 72 hr growth rate) [OECD TG201].

Acute Toxicity

The potential to induce toxicity in mammalian species following acute oral exposure to these chemicals is very low, LD50 values exceed 2,000 mg/kg.

Health

Analysis of C.I. Pigment Red 57 indicated that, in the 28-Day Repeated Dose Toxicity study [OECD TG407], this substance was administered to male and female rats at 0, 100, 300, 1000 mg/kg/day dose by gavage. At 1000 mg/kg/day in males, a decrease of

white blood cell count, total cholesterol and urine pH, also an enlargement of cecum were observed. At 1000 mg/kg in females, an increase of GPT and a decrease of glucose, also an enlargement of cecum were observed. All of those changes recovered within 14 days after cessation of the treatment. No other dose-dependent histopathological changes were observed in any dose groups. No changes in mortality, behavior or toxic effects on the body weight and food consumption were observed in any dose levels and in any sexes. The NOAEL for both sexes is considered to be 300 mg/kg/day.

This substance was not mutagenic in bacteria up to 5,000 ug/plate [OECD TG471, TG472] and 10,000 ug/plate. A chromosomal aberration test tested up to 1.9 mg/mL (10mM) [OECD TG473] was negative except in the 6hr short term test in the presence of an exogenous metabolic activation system. The positive response in the 6 hr short term test was based on the low pH, because the induction of chromosomal aberration was diminished after adjustment of the pH to a neutral range. The result of an unscheduled DNA synthesis up to 187 mg/L was negative. Furthermore, an *in vivo* micronucleus test was negative. Overall, this substance can be considered to be not genotoxic *in vitro* and *in vivo*.

In a Preliminary Reproduction Toxicity Screening Test [OECD TG421], this substance was administrated to male and female rats at 0, 100, 300, 1000 mg/kg/day dose by gavage for 48 days in males and 41 – 46 days (from 14 days before mating to 3 days after parturition) in females. No compound-related dose effects were observed in the copulation index, fertility index, gestation length, number of corpora lutea or implantations, implantation index, gestation index and maternal behavior. As for pups, there were no significant differences in number of offspring or live offspring, sex ratio, the live birth index, the viability index or the body weight. No pups with malformations were found in any groups. No changes in clinical signs and necropsy findings were observed in offspring. From those results, the NOAEL for reproductive and developmental toxicity is considered to be 1000 mg/kg/day.

Conclusion

All endpoints have been satisfied with data, on C Amine and 2 B Acid or through the use of structural surrogates, which are of sufficient quality to conclude that no additional testing is needed. Since these substances are intermediates used only in the production of specific color pigments at a limited number of facilities exposure to these products in use is very limited.

EVALUATION OF DATA FOR QUALITY AND ACCEPTABILITY

The collected data were reviewed for quality and acceptability following the general US EPA guidance (3) and the systematic approach described by Klimisch *et al.* (4). These methods include consideration of the reliability, relevance and adequacy of the data in evaluating their usefulness for hazard assessment purposes. This scoring system was only applied to ecotoxicology and human health endpoint studies per EPA recommendation (5). The codification described by Klimisch specifies four categories of reliability for describing data adequacy. These are:

1. **Reliable without Restriction:** Includes studies or data complying with Good Laboratory Practice (GLP) procedures, or with valid and/or internationally accepted testing guidelines, or in which the test parameters are documented and comparable to these guidelines.
2. **Reliable with Restrictions:** Includes studies or data in which test parameters are documented but vary slightly from testing guidelines.
3. **Not Reliable:** Includes studies or data in which there are interferences, or that use non-relevant organisms or exposure routes, or which were carried out using unacceptable methods, or where documentation is insufficient.
4. **Not Assignable:** Includes studies or data in which insufficient detail is reported to assign a rating, e.g., listed in abstracts or secondary literature.

REFERENCES

1. EPIWIN, Version 3.10, Syracuse Research Corporation, Syracuse, New York.
2. US EPA. (1999). The Use of Structure-Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program. OPPT, EPA.
3. USEPA (1998). 3.4 Guidance for Meeting the SIDS Requirements (The SIDS Guide). Guidance for the HPV Challenge Program. Dated 11/2/98.
4. Klimisch, H.-J., Andreae, M., and Tillmann, U. (1997). A Systematic Approach for Evaluating the Quality of Experimental Toxicological and Ecotoxicological Data. *Regul. Toxicol. Pharmacol.* 25:1-5.
5. USEPA. 1999. Determining the Adequacy of Existing Data. Guidance for the HPV Challenge Program. Draft dated 2/10/99.

I. General Information

CAS Number: 2B Acid (CAS NO.: 88-51-7)
Name: 6-Amino-4-chloro-m-toluenesulfonic acid

CAS Number: C Amine or "C Acid" (CAS NO. 88-53-9)
Name: 2-Amino-5-chloro-p-toluenesulfonic acid

II. Physical-Chemical Data

A1. Melting Point

Test Substance

Test substance: 6-Amino-4-chloro-m-toluenesulfonic acid

Remarks:

Method

Method: Measured

Remarks:

Results

Melting point value: 330 °C

Remarks:

References

Company supplied data

Other

Data is consistent with melting points for the class of pigments and other available measurements

A2. Melting Point

Test Substance

Test substance: 2-Amino-5-chloro-p-toluenesulfonic acid

Remarks:

Method

Method: Estimated

Remarks:

Results

Melting point value: 283.5 °C estimate, Adapted Joback method

Remarks:

References

MPBPWIN v. 1.41 in EPIWIN v 3.10, Syracuse Research Corporation, Syracuse, New York

Other

Data is consistent with melting points for the class of compounds and other available measurements.

B. Boiling Point
Test Substance
Test substance: SOLID
Remarks:

Method
Method:
Remarks:

Results
Boiling point value:
Remarks:

References

Other

C1. Vapor Pressure
Test Substance
Test substance: 2-Amino-5-chloro-p-toluenesulfonic acid and 6-Amino-4-chloro-m-toluenesulfonic acid
Remarks:

Method
Method: Estimation
Remarks: Modified Grain method

Results
Vapor pressure value: 1.55E -008
Temperature:
Remarks:

References
MPBPWIN v1.40 in EPIWIN v3.10, Syracuse Research Corporation,
Syracuse, New York

Other

C2. Vapor Pressure
Test Substance
Test substance: 4-Amino-m-toluenesulfonic acid
Tokyo Kasei Kogyo Co., Ltd.; purity 99.9%
Remarks:

Method
Method: Measured Value
Remarks: 1999

Results
Vapor pressure value: <.00052Pa
Temperature: 100 °C
Remarks:

References

Chemical Inspection and Testing Institute, Japan (1999): report on physical and chemical properties

Other

D. Partition Coefficient**Test Substance**

Test substance: 4-Amino-m-toluenesulfonic acid

Remarks:

Method

Method: OECD TG107 (flask-shaking, no buffer used)

Remarks: 1999, GLP

Results

Log Pow: -.67 at 25 °C

Remarks: sample weight: 1.06mg (= 5mL x 212mg/L)

component of test solution:

condition

case -1 mL -2 mL -3 mL

References**Other**

1-octanol saturated by water 5 10 20

water saturated by 1-octanol 30 25 15

temperature: 25(24-26)°C

revolution: 20/min x 5min

number of replicate: 2

analysis: HPLC

Chemical Inspection and Testing Institute, Japan (1999): report on partition coefficient between 1-Octanol and water

E. Water Solubility**Test Substance**

Test substance: 4-Amino-m-toluenesulfonic acid

Remarks: purity >99%

Method

Method: Measured Value 6 g/L at 20°C pH value : = 3.8

Remarks:

Results

Value: 6.0 g/L

Temperature: 20 °C

Description: Soluble (1000-10000 mg/L)

Remarks:

References

Mitsuboshi Chemical Co., Ltd.: unpublished report

III. Environmental Fate Endpoints

A. Photodegradation

Test Substance

Test substance:

2-Amino-5-chloro-p-toluenesulfonic acid and 6-Amino-4-chloro-m-toluenesulfonic acid

Remarks:

Method

Method:

Estimate

Test type:

Water\sunlight

Remarks:

Results

Temperature:

Degradation Rate

: Half-life

Ozone reaction:

7.20 hours, .6 days (12 Hour day; 1.5×10^6 OH/cm³)

Remarks:

n/a

Conclusions

References

AopWin v1.90 in EPIWIN v3.10, Syracuse Research Corporation, Syracuse, New York, SIDS DOSSIER 4B Acid

Other

A2. Photodegradation

Test substance: 4-Amino-m-toluenesulfonic acid

Remarks:

Method

Method:

Test type:

Estimation

Remarks:

Water

Results

Temperature:

Hydroxyl radicals reaction

OH Rate constant:

Half-life

Ozone reaction: .4 days

Remarks:

Conclusions

References

AopWin v1.90 in EPIWIN v3.10, Syracuse Research Corporation, Syracuse,
New York, SIDS DOSSIER 4B Acid

Other

B. Stability in Water

Test Substance

Test substance: 4-Amino-m-toluenesulfonic acid

Remarks:

Method

Method: OECD Test 111
t1/2 pH4 : > 5 day(s) at 50 °C
t1/2 pH7 : > 5 day(s) at 50 °C
t1/2 pH9 : > 5 day(s) at 50 °C

Test type: abiotic hydrolysis

GLP: no

Remarks: 1999

Results

Half-life: pH 4 >5 days, pH 7 >5 days and pH 9 >5

Percent hydrolyzed in

5 days (120 hs)

at 50 °C :

Remarks:

Conclusions

The test substance has no activity of hydrolysis and is stable at pH 4, pH 7 and pH 9.

Data Quality

Remarks:

References

Chemical Inspection and Testing Institute, Japan (1999): report on physical and chemical properties

C. Biodegradation

Test Substance

Test substance: 4-Amino-m-toluenesulfonic acid
Remarks: purity >99%

Method

Method: OECD Guide-line 301 C "Ready Biodegradability: Modified MITI Test (I)"

Test type: Biological Oxygen Demand (BOD)

GLP: no

Year: 1975

Remarks: Degree of degradation after 28 days (Japanese standard activated sludge)

Control substance : Aniline

Results

Kinetic : 7 day(s) > 40 %

Results: 14 day(s) > 60 %

Remarks:

Conclusions

not biodegradable

Data Quality

Remarks: under test conditions no biodegradation observed

References

This was a well-documented study that followed established guidelines.

Other

Chemical Inspection and Testing Institute, Japan (1999): report on biodegradation, Company supplied data.

D. Transport between Environmental Compartments (Fugacity)

Test Substance

Test substance: 2-Amino-5-chloro-p-toluenesulfonic acid and 6-Amino-4-chloro-m-toluenesulfonic acid
Remarks:

Method

Test type: Estimation
Model used: Level III Fugacity Model; EPIWIN:EQC from Syracuse Research Corporation
Remarks:

Results

Model data and results:	Distribution (%)
Air	4.48 E-005
Water	46.4
Soil	53.5
Sediment	0.0755

Remarks: Since no experimental values were available the physical chemical values utilized in this model were default parameters from within EPIWIN.

Conclusions

References

Meylan, W. (1993). User's Guide for the Estimation Programs Interface (EPI), Version 3.10, Syracuse Research Corporation, Syracuse, New York 13210. The Level III model incorporated in EPIWIN is a Syracuse Research Corporation adaptation of the methodology described by Mackay *et al.* 1996; *Environ. Toxicol. Chem.* **15**(9), 1618-1626 and 1627-1637.

Other

IV. Ecotoxicity

A. Acute Toxicity to Fish

Test Substance

Test substance: 4-Amino-m-toluenesulfonic acid
Remarks: Purity >95%

Method

Method: OECD 203
Test type: Flow through
GLP: yes
Year: 1999
Species/strain: *Oryzias latipes* (Orange Killifish)
Analytical monitoring: yes; Exposure solutions, temperature, pH, dissolved oxygen
Exposure period: 96-Hour
Remarks: A group of 10 fishes were exposed to 10 mg/L, Solvent Control (<.1mg/l) and laboratory water control

Results

Nominal concentration:
Measured concentration:
Endpoint value: 96-hour $LC_{50} > 10$ mg/L
Biological observations:

Statistical methods:
Remarks:

Conclusions

NO abnormal behavior, abnormal respiration nor dad were observed in any dose level

Data Quality

Reliability: Reliable without restrictions
Remarks:

References

Report No. EFA98002, Environment Agency, Japan (1999a): unpublished report

Other

A2. Acute Toxicity to Fish

Test Substance

Test substance: 2-Amino-5-chloro-p-toluenesulfonic acid and 6-Amino-4-chloro-m-toluenesulfonic acid

Remarks:

Method

Method: Estimation

Test type:

GLP:

Year: 2006

Species/strain: fish

Analytical monitoring:

Exposure period:

Remarks:

Results

Nominal concentration:

Measured concentration:

Endpoint value: 96 Hour LC 50 91074.4 mg/L

Biological observations:

Statistical methods:

Remarks:

Conclusions

Data Quality

Reliability:

Remarks:

References

Meylan, W. (1993). User's Guide for the Estimation Programs Interface (EPI), Version 3.10, Syracuse Research Corporation, Syracuse, New York 13210.
The ECOSAR model incorporated in EPIWIN is a Syracuse Research Corporation adaptation of the methodology described by Mackay *et al.* 1996; *Environ. Toxicol. Chem.* **15**(9), 1618-1626 and 1627-1637.

Other

**B. Acute Toxicity to
Aquatic Invertebrates Test**

Substance

Test substance:

4-Amino-m-toluenesulfonic acid
Purity >95%

Remarks:

Method

Method:

Test type:

OECD 202.

GLP:

Static

Year:

Yes

Species/strain:

1999

Analytical monitoring:

Daphnid (*Daphnia magna*)

Exposure period:

No

Remarks:

48 hours

Results

Nominal concentration:

Measured concentration:

10 mg/L

Endpoint value:

48 -hour LC₅₀ >10mg/l,

Reproduction

Biological observations:

Statistical methods:

Remarks:

5 daphnids (4 replicates; 5 organisms per replicate) were exposed to 1 nominal concentrations (10 mg/L) control of DMSO: HCO-40 =9:1 (100mg/L) and laboratory water control

Conclusions

Data Quality

Reliability:

Reliable without restrictions

Remarks:

This was a well-documented OECD guideline study conducted under GLP assurances.

References

Report No. EDI98002, Environment Agency, Japan (1999b): unpublished report
EA Japan (1999) OECD SIDS DOSSIER 4B ACID
Data for Chronic Toxicity to aquatic invertebrates also available

Other

C. Toxicity to Aquatic Plants

Test Substance

Test substance: 4-Amino-m-toluenesulfonic acid
Purity >95%

Remarks:

Method

Method: OECD 201
Test type: Biomass
GLP: Yes
Year: 1999
Species/strain: *Selenastrum capricornutum*
Endpoint basis:
Exposure period: 72 hours
Analytical procedures: Yes
Remarks:

Results

Nominal concentration: 10/mg/L
Measured concentration:
Endpoint value: $EC_{50} > 10 \text{ mg/L}$
NOEC: $> 10 \text{ mg/L}$
Biological observations:
Was control response
satisfactory: Yes
Statistical Methods:
Remarks:

Conclusions

No growth inhibition was observed to green algae up to 10 mg/L

Data Quality

Reliability: reliable with restriction
Remarks:

References

Report No. EDR98002, Environment Agency, Japan (1999c): unpublished report. EA Japan (1999) OECD SIDS DOSSIER 4B ACID

Other

V. Toxicological Data

A. Acute Toxicity

Test Substance

Test substance: 2-Amino-5-chloro-p-toluenesulfonic acid and 6-Amino-4-chloro-m-toluenesulfonic acid

Remarks:

Purity was unknown

Method

Method: Acute lethality; Other

Test type: LD₅₀ estimate

GLP: No (Pre-GLP)

Year: 1968

Species/strain: Rat/unknown

Route of exposure: Oral gavage

Dose levels: Unknown

Remarks:

Results

Value: LD₅₀ = >7,500 mg/kg 2B acid

Deaths at each dose:

Remarks:

Conclusions

Material would be considered as not toxic.

Data Quality

Reliability: Reliable with restrictions

Remarks:

References

Other

Acute toxicity

Test substance: 4-Amino-m-toluenesulfonic acid
99%Purity

Remarks:

Method

Method: Acute lethality; Other
Test type: LD₅₀ estimate
GLP: Yes
Year: 1996
Species/strain: Rat
Route of exposure: Oral gavage
Dose levels: 0,100,250,500,1000,2000 mg/kg/day
Remarks:

Results

Value: LD₅₀ = >2,000 mg/kg.
Deaths at each dose:
Remarks:

Conclusions

Material would be considered as not toxic.

Data Quality

Reliability: Reliable without restrictions
Remarks:

References

Ministry of Health & Welfare, Japan (1996a): Toxicity Testing Reports of Environmental Chemicals, vol.4 p. 99-106, "Twenty-eight-day Repeat Dose Oral Toxicity Test of 2-Amino-5- methylbenzenesulfonic acid in Rats".

Other

**Repeated Dose Toxicity Test
Substance**

Test substance: 4-Amino-m-toluenesulfonic acid
Remarks: Commercial purity 98%

Method

Method: OECD 407
Test type: Repeat Dose
GLP: Yes
Year: 1996
Species/strain: Rat Male and Female
Route of exposure: Gavage
Duration of test: 42 days
Exposure levels: 0, 100, 300 or 1,000 mg/kg
Sex: Male and female
Exposure period: 28 days
Post-exposure
observation period:
Remarks:

Results

NOAEL (NOEL): 300 mg/kg/day
No change in mortality and behavior were observed in any groups.
body weight and food consumption: No toxic effect was observed in any groups. urinary findings: Increase of specific gravity and decrease of pH were observed in 1000 mg/kg males. However no related change was observed in other findings. hematological findings: Slight decrease of white blood cell count (due lymphopenia) were observed in 1000 mg/kg males. No pathological change was observed in the lymphatic tissues, such as marrowcyte, thymus, lymphknote and spleen. blood chemical finding: Slight increase of GPT in females, slight decrease of total cholesterol in males and slight decrease of glucose in females were observed in 1000 mg/kg group. However, including liver, no pathological change was observed in any of related organs. According to the author, the change is within normal range, based on their other study data. necropsy finding: Slight enlargement of cecum was observed in one male and one female in 1000 mg/kg group. However no diarrhea and no growth abnormalities were observed. weight of organs: Decrease of thymus weight in 100 mg/kg and increase of spleen weight in all dose levels in female were observed. However those changes were no relation with dose levels.
remark: All of above changes returned to normal during 14 days recovery period.

Conclusions

Test substance is not significantly toxic

Data Quality

Reliability: Reliable without restriction Remarks:

References: Ministry of Health & Welfare, Japan (1996a): Toxicity Testing Reports of Environmental Chemicals, vol.4 pp. 99-106, "Twenty-eight-day Repeat Dose Oral Toxicity Test of 2-Amino-5-methylbenzenesulfonic acid in Rats".

C. Genetic Toxicity - Mutation

Test Substance

Test substances: 2-Amino-5-chloro-p-toluenesulfonic acid and 6-Amino-4-chloro-m-toluenesulfonic acid

Remarks:

Method

Method: In Vitro Mutagenicity
Test type: Ames
GLP: Unknown
Year: 1985 C Amine, 1988 2B Acid
Species/strain: Salmonella typhimurium
Metabolic activation: Yes
Concentration tested:
Remarks:

Results

Result: Negative
Cytotoxic
concentration:
Precipitation
concentration: Negative
Genotoxic effects
With
activation: Negative
Without
activation:
Statistical methods:
Remarks:

Conclusions

Reliable with restrictions, studies are well documented.

Data Quality

Reliability: Hidesuke Shimizu et al., JPN J. Ind. Health, Vol27, pp. 400-419 (1985) (C Amine), Yoshimi, N., Sugie, S., Iwata, H et al. Mutation Research Vol. 206, pp.183-191, 1988 (2B Acid)
Remarks:

References

C. Genetic Toxicity - Mutation

Test substance: 4-Amino-m-toluenesulfonic acid Remarks: 98% pure

Method

Method: OECD 471, 472

Test type:	Ames
GLP:	Yes
Year:	Japan (1996)
Species/strain:	Salmonella typhimurium
Metabolic activation:	With and without
Concentration tested:	5000 ug/plate with and without activation
Remarks:	

Results

Result:	Negative in all bacterial strains with and without activation
Cytotoxic concentration:	
Precipitation concentration:	
Genotoxic effects	
With activation:	Negative
Without activation	Negative
Statistical methods:	
Remarks:	

Conclusions

Data Quality

Reliability:	Reliable without restriction	Remarks:
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References

Report No. CTL/P/1999, Ecological and Toxicological Association of Dyes and Organic Pigments Manufacturers, unpublished report.

Other

D. Genetic Toxicity – Chromosomal Aberrations

Test Substance

Test substance: 4-Amino-m-toluenesulfonic acid
Commercial purity 99%

Remarks:

Method

Method:
Test type: OECD 473
GLP: Cytogenetics Assay
Year: Yes
Species/strain: 1996
Exposure period: Chinese Hamster CHL Cells
Remarks:

Results

Result:
Genotoxic effects: Negative
Concentration tested: Negative
Statistical methods: 0, 16, 80, 400, or 2000 ug/mL
Remarks:

Conclusions

This chemical induces weak chromosomal aberration to CHL/IU cell with an exogenous metabolic activation system. However, origin of the aberration is due to the acidity, but not due to physiological DNA damage. (The low acidity effect is reported in [T.Morita et al., Mutation Res, 268, 297 1992].)

Data Quality

Reliability:
Remarks:

Reliable without restriction

References**Other**

Ministry of Health & Welfare, Japan (1996c): Toxicity Testing Reports of Environmental Chemicals, vol.4 p111-114, "In Vitro Chromosomal Aberration Test of 2-Amino-5-methylbenzenesulfonic acid on Cultured Chinese Hamster Cells".

E. Developmental Toxicity

Test Substance

Description included in OECD 422 study described above

Test substance:

Remarks:

Method

Method:

GLP:

Year:

Species/strain:

Sex:

Route of exposure:

Exposure levels:

Actual doses received:

Exposure period:

Duration of test:

Remarks:

Results

Maternal toxicity

NOEL:

NOEL for

teratogenicity:

NOEL for fetotoxicity:

Parental toxic

responses:

Fetal toxic responses

dose:

Statistical Methods:

Remarks:

Conclusions

Data Quality

Reliability:

Remarks:

References

Other

F. Toxicity to Reproduction

Test Substance

Test substance: 2-Naphthalenecarboxylic acid, 3-hydroxy-4-[(4-methyl-2-sulfophenyl)azo]-, calcium salt

Remarks: Commercial purity 98%

Method

Method: OECD 421

GLP: Yes

Year: 1999

Species/strain: Rat

Sex: male and female

Route of exposure: gavage

Exposure levels: 0,100,300 or 1000 mg/kg

Exposure period: males 48 days including /females 41-48 days

Duration of test:

Remarks:

Results

Maternal toxicity NOEL: Parental, 1000 mg/kg/day

Parental toxic responses:

Fetal toxic responses dose:

Statistical Methods:

Remarks: No effects were observed in the copulation index, fertility index, gestation length, number of corpora lutea or implantations, implantation index, gestation index, parturition or maternal behavior. There were no significant differences in number of offspring or live offspring, sex ratio, the live birth index, the viability index and the body weight. No abnormal findings related to the test substance were noted for external features, clinical signs, or on necropsy finding for the offspring. No pups with malformation were found in any group. No change in clinical signs and necropsy finding were observed in offspring.

Conclusions

Data Quality

Reliability: Reliable without restriction

Remarks:

References

Other

Ministry of Health & Welfare, Japan (1999): Toxicity Testing Reports of Environmental Chemicals, vol.7 p163-171, "Preliminary Reproduction Toxicity Screening Test of 2-Amino-5-methylbenzenesulfonic acid by Oral Administration in Rats".

Acute toxicity

Test substance:

2-Naphthalenecarboxylic acid, 3-hydroxy-4-(5-chloro-4-methyl-2-sulfophenyl)azo]-, Barium salt and 2-Naphthalenecarboxylic acid, 3-hydroxy-4-(5-chloro-4-methyl-2-sulfophenyl)azo]-, Calcium salt

Remarks:

Method

Method:

Irritation to the rabbit eye

Test type:

eye irritation

GLP:

unknown

Year:

1972

Species/strain:

rabbit

Route of exposure:

Dose levels:

Remarks:

Results

Value:

negative

Deaths at each dose:

Remarks:

Conclusions**Data Quality**

Reliability:

unassignable

Remarks:

References

Company data

Other

Acute toxicity

Test substance:

2-Naphthalenecarboxylic acid, 3-hydroxy-4-(5-chloro-4-methyl-2-sulfophenyl)azo]-, Barium salt and 2-Naphthalenecarboxylic acid, 3-hydroxy-4-(5-chloro-4-methyl-2-sulfophenyl)azo]-, Calcium salt

Remarks:

Method

Method:

Skin irritation to the rabbit

Test type:

Skin irritation

GLP:

unknown

Year:

1972

Species/strain:

rabbit

Route of exposure:

Dose levels:

Remarks:

Results

Value:

negative

Deaths at each dose:

Remarks:

Conclusions**Data Quality**

Reliability:

unassignable

Remarks:

References

Company data

Other

